Contains No CBI

RHÔNE-POULENC

8EHQ-92-12099
INIT
88920010337

(A)

RHÔNE-POULENC INC.
CN 7500, CRANBURY, NJ 08512-7500
TELEPHONE: (609) 395-8300

September 4, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
P 713 002 196

Document Processing Center (TS-790)
Attn: Section 8(e) Coordinator (CAP Agreement)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID NO.: 8ECAP - 0004

RP CAP REPORT NO.: RPS - 0184

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN5266, Princeton, NJ 08543-5266) and its subsidiaries, the attached report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA (8ECAP - 0004).

The enclosed report provides information on the following chemical substance:

Chemical Identity:	Pentaerythritol triacrylate (PETA) (Coded as C-253 in report)
CAS Registry No:	3524-68-3
CAS Registry Name:	2-Propenoic acid, 2-(hydroxymethyl)-2-[((1-oxo-2-propenyl)oxy)methyl]-1,3-propanediyl ester

3/10/95

V. METHODS:

A. Test Design:

Doses for the preliminary range-finding screen were administered as follows:

Number of Animals M	Number of Animals F	Dose Level (mg/kg) (C-253)	Dose Volume (ml/kg C-253 in DMSO)	Conc. (% w/w C-253 in DMSO)
1	1	3	0.27	1.0
1	1	10	0.90	1.0
1	1	30	2.71	1.0
1	1	100	9.02	1.0
1	1	300	27.1	1.0
1	1	3	0.027	10.0
1	1	10	0.09	10.0
1	1	30	0.27	10.0
1	1	100	0.89	10.0
1	1	300	2.7	10.0

Based on mortality observed at these dose levels; doses for the LD_{50} determination were administered as follows:

Number of Animals M	Number of Animals F	Dose Level (mg/kg) (C-253)	Dose Volume (ml/kg C-253 in DMSO)	Conc. (% w/w C-253 in DMSO)
5	5	3	0.026	10.0
5	5	10	0.088	10.0
5	5	30	0.26	10.0
5	5	100	0.88	10.0

B. Preparation of Test and Control Material:

Vehicle: DMSO

Procedure: Appropriate amounts of the test material were weighed and placed in an appropriate container and vehicle was added to achieve the total desired weight.

Control Material (DMSO) was adminstered as received, no mixture was required.

V. METHODS (cont.):

C. Administration of Test and Control Material:

The test and control material were administered by intraperitoneal injection using a syringe of appropriate size, fitted with a 21 gauge needle.

D. Duration of Study:

Range-finding: 7 days

LD_{50} Determination: 14 days

E. Experimental Evaluation:

Range finding: Animals were observed for viability twice daily for fourteen days and deaths were recorded.

LD_{50} Determination:

Viability Checks: Twice Daily

Observations for Pharmacologic and Toxicologic Signs:

Approximately 1, 2 and 4 hours after dosing and daily thereafter for fourteen days.

Neurologic Examination:

Approximately 1, 2, 4 and 24 hours after dosing in all animals

Survivors at the 30 mg/kg dose level were observed daily through Day 14

Animals at the 10 mg/kg dose level which exhibited neurologic abnormalities at 24 hours were observed daily thereafter through Day 7; animals which continued to exhibit abnormalities at Day 7 were observed daily through Day 14.

Body Weights:

Pretest (weights used for calculation of doses)

Day of Dosing (just prior to dosing)

Day 7 and 14

Terminal: Any animals which did not survive for 14 days were weighed at the time of death or at the time they were found dead.

V. METHODS (cont.):

F. Postmortem Examination:

No postmortem examinations were made on animals used for range-finding screens. The following was done for all other animals: Gross postmortem examinations were performed on all animals which died or were found dead during the study. All animals surviving at termination of the observation period (Day 14) were killed by carbon dioxide inhalation and examined grossly. All abnormalities were recorded but no tissues were saved.

G. Reference - LD_{50} Calculation:

Miller, Lloyd C. and M.L. Tainter., Estimation of the ED_{50} and Its Error by Means of Logarithmic-Probit Graph Paper, Proc. Soc. Exp. Biol. Med. 57: 261-264 (1944).

VI. RESULTS AND DISCUSSION:

A. Mortality

Dose levels and mortality for the preliminary range-finding study were as follows:

Dose Level (mg/kg)	Mortality
3	0/4
10	1/4
30	3/4
100	4/4
300	4/4

- from 10%
- 2 at 10%, 1 at 10%.

Dose levels, mortality and the estimated LD_{50} with 95% confidence limits were as follows:

Dose Level (mg/kg)	Males	Females	Total	Time to Death
3	0/5	0/5	0/10	-
10	0/5	0/5	0/10	-
30	5/5	3/5	8/10	23.5 Hr-Day 6
100	5/5	5/5	10/10	4 Hr-5.5 Hr
LD_{50} (mg/kg):	18.5	27	25	
95% Confidence Limits (mg/kg):	a	2-52	12.5-37.5	

Time to death was generally dose-related.

[a]Confidence limits could not be calculated.

B. Body Weights (Table I)

Most animals which died after receiving 30 mg/kg exhibited substantial antemortem weight losses. Weight gains in survivors at this dose level and in males at the 10 mg/kg dose level were lower than those in control animals. Two of the 5 females in the 10 mg/kg dose group exhibited weight losses at 7 or 14 days. Gains in the remaining 3 animals in this group and in all 10 animals in the 3 mg/kg group were comparable to those of control animals.

VI. RESULTS AND DISCUSSION (cont.):

C. Neurologic Signs (Table II)

Signs seen in all or most animals in the 30 and 100 mg/kg groups were ataxia, flaccid limb and body tone and abnormal righting and visual placing reflexes. A few animals which died also exhibited convulsions, abnormal startle, pupil or corneal reflexes and uncoordinated eye movements prior to death. The two survivors in the 30 mg/kg group continued to exhibit ataxia, body and limb flaccidity and/or abnormal righting and visual placing reflexes throughout most or all of the 14-day post dose observation period. One also exhibited compulsive biting between Days 7 and 14.

Neurologic abnormalities were noted in 5 of the 10 animals in the 10 mg/kg group (3 males, 2 females) and consisted of ataxia, flaccid limb and body tone and abnormal righting and visual placing reflexes. The males were free of neurologic abnormalities by Day 5; one of the females was free of abnormalities by Day 10 but the second continued to exhibit an abnormal righting reflex through termination of the study (Day 14).

No neurologic abnormalities were observed in animals which received 3 mg/kg of C-253.

D. Pharmacologic and Toxicologic Signs (Table III)

Animals in the 30 and 100 mg/kg groups exhibited a number of abnormalities, including decreased activity and respiration rates and apparent severe abdominal discomfort (writhing) on the day of dosing. The latter observation is consistent with the lesions described below, which were seen upon postmortem examination. Similar signs were also noted in some animals in the 10 mg/kg group. The two survivors (females) in the 30 mg/kg group and two of the five females in the 10 mg/kg group exhibited a number of abnormalities throughout the post-dose period. These included decreased activity and

VI. RESULTS AND DISCUSSION (cont.):

respiration rates, decreased food consumption, urinary and fecal staining, unthrifty coat and other signs as detailed in Table III.

Animals in the 3 mg/kg group were free of abnormalities except for the presence of swollen eyelids and/or ocular discharge in two animals between Days 8 and 14. This was not considered to represent an effect of the test material.

E. Postmortem Examination (Table IV)

All animals which died and those which were killed after 14 days exhibited a large number of postmortem abnormalites, most notably in the abdominal viscera. Most of these appeared to represent irritation and/or infectious sequelae resulting from intraperitoneal injection of the vehicle and/or test material.

Carol S. Auletta, B.A., D.A.B.T.
Study Director — Date 7/27/82

for Geoffrey K. Hogan, Ph.D., D.A.B.T.
Vice President of Toxicology — Date 7/27/82

Craig Lamb, B.A.
Manager, Quality Assurance — Date 7/27/82

TABLE I

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

BODY WEIGHTS (GRAMS) AND TIME FOUND DEAD

Dose Level mg/kg	Animal No. & Sex	Pretest Weights		Interim Deaths			Survivors			
		Pre-test	Day of Dosing	Terminal Weight	Time Found Dead[a]	Chg[b]	Day 7	Chg[b]	Day 14	Chg[b]
Controls (DMSO)	5948 M	258	273				311	53	357	99
	5944 M	237	255				295	58	335	98
	5923 M	228	242				279	51	308	80
	5956 M	212	226				265	53	304	92
	5949 M	218	228				273	55	312	94
	5971 F	224	238				239	15	248	24
	5977 F	213	224				227	14	234	21
	5999 F	207	207				218	11	228	21
	5992 F	224	239				230	6	243	19
	5984 F	225	234				234	9	238	13
3	5930 M	236	252				286	50	316	80
	5927 M	243	260				308	65	348	105
	5915 M	241	254				286	45	326	85
	5941 M	257	274				321	64	372	115
	5960 M	244	254				286	42	329	85
	5988 F	227	237				233	6	248	21
	6007 F	228	239				240	12	248	20
	5981 F	214	221				224	10	224	10
	5982 F	213	224				227	14	242	29
	5994 F	225	232				232	7	251	26
10.0	5922 M	231	239				267	36	302	71
	5955 M	233	250				264	31	317	84
	5957 M	229	244				271	42	304	75
	5953 M	238	253				263	25	325	87
	5951 M	234	245				262	28	303	69
	5983 F	228	234				236	8	248	20
	6004 F	230	236				191	-39	241	11
	5978 F	220	230				228	8	241	21
	5969 F	223	230				232	9	243	20
	5966 F	220	231				228	8	204	-16
30	5925 M	222	233	231	23.5 Hr					
	5954 M	222	236	184	Day 5	-38				
	5921 M	237	249	199	Day 4	-38				
	5964 M	236	252	194	Day 5	-42				
	5959 M	243	259	210	Day 4	-33				
	6008 F	210	216				193	17	240	30
	5967 F	219	227	188	Day 6	-31				
	5970 F	208	217				211	3	246	38
	5980 F	222	233	194	Day 5	-28				
	5997 F	214	218	222	Day 2	8				
100	5961 M	227	242	237	4 Hr					
	5916 M	226	242	234	4 Hr					
	5947 M	239	253	246	4 Hr					
	5936 M	234	247	241	4 Hr					
	5952 M	210	222	219	4 Hr					
	5998 F	228	241	235	4 Hr					
	5974 F	217	229	225	5.5 Hr					
	6002 F	213	221	218	5.5 Hr					
	5991 F	226	235	230	5.5 Hr					
	5973 F	214	225	219	4 Hr					

[a]See Table III for type of death.
[b]Change from pretest weight (grams). Weight changes were not calculated for animals that died on the day of dosing or overnight after dosing (i.e., animals found dead at the 24 hour observation).

TABLE II

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

SUMMARY OF NEUROLOGIC SIGNS[a]

Observations	Interval: Day: Hr: / Dose (mg/kg)	Animals Found Dead: 1 Hr M/F	2 Hr M/F	4 Hr M/F	1 Day 24 Hr M/F	2 Day M/F	3 Day M/F	4 Day M/F	5-7 Day M/F	Survivors: 1 Hr M/F	2 Hr M/F	4 Hr M/F	1 Day 24 Hr M/F	2 Day M/F	3 Day M/F	4 Day M/F	5-7 Day M/F	8-14 Day M/F
	Controls (1/12/82)	No observable abnormalities (observed through 24 hours)																
	3	No observable abnormalities (observed through 24 hours)																
Ataxia	10	-	-	-	-	-	-	-	-	-	-	-	1/-	-	-	-	-/2	-/2
Body Tone-Flaccid		-	-	-	-	-	-	-	-	-	-	-	2/-	1/-	2/-	2/-	-/2	-/1
Limb Tone-Flaccid		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/2	-/1
Abnormal Righting Reflex		-	-	-	-	-	-	-	-	-	-	1/-	-	-	-	-	-/2	-/2
Abnormal Visual Placing Reflex		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/2	-/2
Total Number of Animals[b]		-	-	-	-	-	-	-	-	5/5	5/5	5/5	5/5	2/2	2/2	2/2	2/2	-/2
Convulsions	30	-	-	-	-/1	-	-	-	-									
Compulsive Biting		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/1	-/1
Uncoordinated Eye Movements		-	-	-/1	-/1	-/1	-/1	-/1	-	-	-	-	-	-	-	-	-	-
Pelvic Elevation		-	-	-	-	-	-	-	-	-	-	-/1	-	-	-	-	-	-
Ataxia		1/-	3/1	5/3	2/2	3/2	4/2	2/2	-/1	-	-	-/2	-/2	-/2	-/2	-/2	-/2	-/1
Body Tone-Flaccid		-	2/-	4/1	3/2	4/1	4/2	2/1[c]	-/1	-	-	-/1	-/1	-/1	-/2	-/1	-/1	-/1
Limb Tone-Flaccid		-	1/-	1/-	1/1	2/1	4/1	2/1	-/1	-	-	-	-/1	-/1	-/2	-	-	-
Toe Pinch		-	-	1/-	-/1	-	1/-	-	-	-	-	-	-	-	-	-	-	-
Pupil-No Light Response		-	-	-	-/1	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Righting Reflex		4/-	5/2	5/3	4/3	4/2	4/2	2/2	-/1	-	-	-/2	-/2	-/2	-/2	-/1	-/2	-/2
Abnormal Visual Placing Reflex		1/-	3/-	3/1	2/2	3/1	4/1	2/1	-/1	-	-	-	-/2	-	-/1	-/1	-	-
Abnormal Corneal Response		-	-	-	-/1	-	-	-	-	-	-	-	-	-	-	-	-	-
Abnormal Startle Reflex		-	-	1/-	-/1	-	1/-	1/-	-/1	-	-	-	-	-	-	-	-	-
Death		-	-	-	1/-	-/1	-	2/-	2/2	-	-	-	-	-	-	-	-	-
Total Number of Animals		5/3	5/3	5/3	4/3	4/2	4/2	2/2	-	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2
Convulsions	100	-	-	-/1	-	-	-	-	-	No Survivors								
Uncoordinated Eye Movements		-	-/1	-/3	-	-	-	-	-									
Pelvic Elevation		-/1	-/1	-	-	-	-	-	-									
Ataxia		5/5	5/5	-/2	-	-	-	-	-									
Body Tone-Flaccid		3/1	4/4	-/3	-	-	-	-	-									
Limb Tone-Flaccid		-	3/1	-/3	-	-	-	-	-									
Toe Pinch		-	1/2	-/3	-	-	-	-	-									
Pupil-No Light Response		-	-	-/1	-	-	-	-	-									
Abnormal Righting Reflex		5/5	5/5	-/3	-	-	-	-	-									
Abnormal Visual Placing Reflex		1/-	4/2	-/3	-	-	-	-	-									
Abnormal Startle Reflex		-	-/1	-/3	-	-	-	-	-									
Death		-	-	5/2	-/3	-	-	-	-									
Total Number of Animals		5/5	5/5	-/3	-	-	-	-	-									

[a]Numbers represent number of males and females out of 5 per sex, or of those surviving which exhibited signs one or more times during interval.
[b]Numbers from Days 2 to 14 indicates number of animals evaluated.
[c]Body tone could not be evaluated in one female due to a distended abdomen.

TABLE III

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

SUMMARY OF PHARMACOLOGIC AND TOXICOLOGIC SIGNS

Observations	Dose (mg/kg)	Interval: Day: / Hr: 1 / 2 / 4 / 24	Survivors 1	2	3	4	5-7	8-14	Time Last Observed
		M/F / M/F / M/F	M/F	M/F	M/F	M/F	M/F	M/F	
	Controls	No observable abnormalities							
Ocular Discharge	3	- - -	-	-	-	-	-	1/-	Day 8
Swollen Eyelids		- - -	-	-	-	-	-	2/-	Day 14
Total Number of Animals		5/5 5/5 5/5	5/5	5/5	5/5	5/5	5/5	5/5	
Nasal Discharge	10	- - -	-/1	-	-	-/1	-/1	-	Day 7
Hypopnea		- - -	-	-	-	-	-	-/1	Day 14
Ocular Discharge		- - -	-	-	-	-	-/1	-	Day 6
Urinary Staining		- - -	-	-	-	-	-/2	-/1	Day 14
Fecal Staining		- - -	-	-	-	-/1	-/1	-/1	Day 9
Unthrifty Coat		- - -	-	-	-	-/2	-/1	-/2	Day 14
Soft Stool		- - -	-	-	-	-	-/1	-/1	Day 8
Hypoactivity		1/- 4/1 4/4	3/2	3/2	3/2	2/2	1/2	-/2	Day 14
Food Consumption Decrease		- - -	-	-	1/2	1/2	1/2	-/2	Day 14
Eye(s) Swollen		- - -	-	-	-	-	-	2/-	Day 14
Blanching		- - -	-	-	-	-	-/1	-	Day 7
Emaciated		- - -	-	-	-	-	-	-/2	Day 9
Abdominal Writhing		- - -/2	-	-	-	-	-	-	4 Hr
Distended Abdomen		- - -	-	-	-	-	-	-/1	Day 14
Total Number of Animals		5/5 5/5 5/5	5/5	5/5	5/5	5/5	5/5	5/5	

[a]Numbers represent number of males and females which exhibited signs one or more times during interval.
-:indicated observation not present.

TABLE III (cont.)

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

SUMMARY OF PHARMACOLOGIC AND TOXIC SIGNS[a]

Observations	Dose (mg/kg)	Animals Found Dead								Survivors									Time Last Observed
Interval: Day:					1	2	3	4	5-7				1	2	3	4	5-7	8-14	
Hr:		1	2	4	24					1	2	4	24						
		M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	M/F	
Prostration	30	-	-	-	-/1	-	-	-	-										
Nasal Discharge		-	-	-	-	1/-	1/-	-	-	-	-	-	-	-	-	-	-	-	
Oral Discharge		-	-	-	-	1/-	1/-	-	-	-	-	-	-	-	-	-	-	-	
Hypopnea		2/1	5/2	5/3	2/1	4/1	4/2	2/2	-/1	-	-	-/2	-/2	-/2	-/2	-/2	-/2	-/2	Day 14
Dyspnea		-	-	-	-/1	-	-	-	-	-	-	-	-	-	-	-/1	-	-	Day 4
Ocular Discharge		-	-	-	-/1	-	1/1	-	-	-	-	-	-	-	-	-	-	-	
Soft Stool		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Abdominal Writhing		-	5/3	5/3	-	-	-	-	-	-	-/2	-/2	-	-	-	-	-/1	-	Day 5
Urinary Staining		-	-	-	-	-	-/1	-/1	-/1	-	-	-	-	-/1	-/2	-	-/2	-/2	4 Hr
Fecal Staining		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/1	-	-	Day 7
Staining of Ano-Genital Area		-	-	-	-	-	-	1/1	-	-	-	-	-	-	-	-	-/2	-	Day 4
Unthrifty Coat		-	-	-	-	-	-	1/-	-	-	-	-	-	-	-	-	-/1	-/2	Day 14
No Stool		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/1	Day 9
Piloerection		-	-	-/1	-	-	-	1/-	-	-	-	-	-	-	-	-	-	-	
Hypothermia		-	-	-	-/1	-	-	1/1	-/1	-	-	-	-	-	-	-	-	-	
Alopecia on Abdomen or Ano-Genital Area		-	-	-	-	-	-	-	-/1	-	-	-	-	-	-	-	-/1	-/2	Day 14
Hypoactivity		4/2	5/3	5/3	4/2	4/2	4/2	2/2	-/1	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2	Day 14
Food Consumption Decrease		-	-	-	-/1	-	4/2	2/2	-/1	-	-	-	-	-	-/2	-/2	-/2	-/2	Day 13
Emaciated		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/1	Day 8
Distended Abdomen		-	-	-	-	-	-	-/1	-	-	-	-	-	-	-	-	-	-/2	Day 14
Blanching		-	-	-	-	-	-	-	-/1	-	-	-	-	-	-	-	-	-	
Necrotic Tail		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-/1	-/1	Day 14
Eyes Partially Closed		-	-	-	-	-	-	1/-	-	-	-	-	-	-	-	-	-	-	
Death		-	-	-	1/-	-/1	-	2/-	2/2	-	-	-	-	-	-	-	-	-	
Total Number of Animals		5/3	5/3	5/3	4/3	4/2	4/2	2/2	-	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2	-/2	
Hypopnea	100	4/4	5/5	-/2	-														
Dyspnea		-	-	-/1	-														
Ocular Discharge		-	-	-/1	-														
Hypothermia		-	-	-/2	-														
Hypoactivity		5/5	5/5	1/2	-														
Abdominal Writhing		2/5	5/5	-/3	-														
Prostration		-	-	-/1	-														
Death		-	-	5/2	-/3														
Total Number of Animals		5/5	5/5	-/3	-														

[a]Numbers represent number of males and females which exhibited signs one or more times during interval.
-:indicates observation not present.

TABLE IV

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

NECROPSY OBSERVATIONS

SURVIVORS[a]

Necropsy Observations	ANIMAL	Controls (1/12/82) Males					Controls (1/12/82) Females					3 mg/kg Males					3 mg/kg Females					10 mg/kg Males					10 mg/kg Females					30 mg/kg Females	
	NUMBER	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	6	5	5	5	5	5	5	5	5	5	6	5	6	5
		9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	0	9	9	9	9	9	9	9	9	9	0	9	0	9
		4	4	2	5	4	7	7	9	9	8	3	2	1	4	6	8	0	8	8	9	2	5	5	5	5	8	0	7	6	6	0	7
		8	4	3	6	9	1	7	9	2	4	0	7	5	1	0	8	7	1	2	4	2	5	7	3	1	3	4	8	9	6	8	0
Swollen Eye(s)															X	X						X			X							
Urinary Staining																																
Alopecia[b]																										X				X	X	X
Distended Abdomen																															X	X
Necrotic Tail																										X				X	X	X
																																X
Lungs:																																
dark red foci			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
dark red																																
bright red																										X						
mottled dark red			X			X	X	X		X		X			X		X	X	X	X									X			
mottled pale red												X		X																		X
Liver:																																
rounded edges									X						N.O.A.								X		X	X		X		X	X	
white patch																											X					
adhered to diaphram																											X				X	X
Stomach:																																
adhered to spleen and liver					N.O.A.										N.O.A.										X						N.O.A.	
Large Intestine:																																
distended					N.O.A.										N.O.A.															X	X	
green fluid																														X	X	
Spleen:																																
white membranous covering					N.O.A.								X												X			X			N.O.A.	
Adrenals:																																
pale red					N.O.A.														X			X			X			X		X	X	

[a]Survivors: animals were sacrificed at termination of the study (Day 14).
[b]Alopecia of the abdomen or ano-genital area.
X=Observation present; N.O.A.=No observable abnormalities.

TABLE IV (cont.)

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-253

NECROPSY OBSERVATIONS

ANIMALS FOUND DEAD

Necropsy Observations	ANIMAL NUMBER	30 mg/kg Males					30 mg/kg Females					100 mg/kg Males					100 mg/kg Females				
		59251	59454	59121	59469	59559	59674	59807	59970			59961	59916	59743	59636	59252	59978	59704	59021	59915	59737
Ocular Discharge		X		X	X	X															
Nasal Discharge				X		X															
Urinary Staining					X		X	X													
Alopecia-Abdomen or Ano-Genital Area							X														
Distended Abdomen																					
Lungs:																					
pale red		X		X			X					X	X	X	X			X	X	X	
bright red			X		X	X		X	X							X	X	X	X		X
dark red foci																					
mottled tan														X							
mottled bright red									\				X								
Liver:																					
thick edges				X																	
rounded edges																					
adhered to diaphragm																					
pale red									X								X			X	
Stomach:																					
dark red foci		X																			
walls red		X							X			X	X	X	X	X		X	X	X	X
thickened			X																		
wrinkled						X															
distended					X			X													
brown/yellow/green fluid and or substance			X	X	X	X	X	X													
Small Intestine:																					
red walls			X	X					X									X	X	X	X
distended					X		X	X													
mottled red					X		X	X													
orange/yellow/green fluid			X		X			X	X									X	X	X	
brown fluid				X		X	X														
Large Intestine:																					
red walls			X												N.O.A.						
mottled red					X		X	X													
distended					X			X													
contents hard							X														
green fluid																					
brown fluid			X	X	X	X		X													
Spleen:																					
mottled pale red								X									N.O.A.				
Adrenals:																					
dark red/red		X	X		X	X	X	X	X			X	X	X	X	X	X	X			
large							X														
mottled dark red																					X
Testes:																					
found in body cavity		X										N.O.A.									
Uterus:																					
brown fluid							X										N.O.A.				
Body Cavity:																					
yellow fluid		X										X	X	X	X	X	X			X	X
red fluid				X				X	X									X	X		
yellow substance adhered to walls and viscera				X		X															
brown fluid							X														

[a]Animals found dead; see Table I for time of death.
X=Observation present; N.O.A.=No observable abnormalities.

(2)

The title of the enclosed report is:

An Acute Intraperitoneal Toxicity Study in Rats

The following is a summary of the adverse effects observed in this report.

> The intraperitoneal LD50 (with 95% confidence limits) in rats was 25 (12.5-37.5) mg/kg for both sexes combined. Clinical signs of toxicity seen in animals surviving to study termination included ataxia, body and limb flaccidity, abnormal righting and visual placing reflexes. Males were free of signs by Day 5, but one female exhibited abnormal righting reflex throughout the study.

RPI does not claim any portion of the information in this submission to be TSCA confidential business information (TSCA CBI).

One TSCA Section 8(e) notice was made on this chemical. This notice was submitted to EPA on August 6, 1982 by Celanese, but we are unable to find a Document Control Number in our files for the submission. RPI is also submitting other studies on this material under the CAP agreement; see RP CAP Report Nos. RPS-0185, RPS-0190, and RPS-0244.

On August 15, 1985, Celanese submitted to EPA all available toxicity data on the multifunctional acrylates. However, RPI does not have a detailed list in our records of the reports that were submitted. Therefore, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to Dr. Glenn S. Simon, Director of Toxicology at (919)549-2222 (Rhône-Poulenc, P.O. Box 12014, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709).

Sincerely,

Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
(609)860-3589

CEMjr/mm
Enclosures

- Acrylates-Multifunctional-PETA
C-253

CAP ID No. S-LT-PW0087
Reviewed for Sec. 8 (e)
Compliance Program
On 10/8/91 By

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 6817-81

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

Test Material: C-253

Submitted to: Celanese Corporation
New York, New York

Date: July 28, 1982

I. INTRODUCTION

An acute intraperitoneal toxicity study in rats with C-253 was conducted for the Celanese Corporation at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873. The purpose of this study was to evaluate the acute toxicity of the test material when administered by intraperitoneal injection to rats; to determine the intraperitoneal LD_{50} of the material; and to determine whether neurologic effects could be produced with acute administration.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data.

II. DATES OF STUDY:

Range finding:

Animal Receipt:	December 8, 1981
Initiation (Dosing):	December 30, 1981
Termination:	January 6, 1982
Animal Receipt:	December 8, 1981
Initiation (Dosing):	January 7, 1982
Termination:	January 14, 1982

LD_{50} Determination:

Animal Receipt:	January 12, 1982
Initiation (Dosing):	January 21, 1982
Termination:	February 4, 1982

III. STUDY PERSONNEL:

Study Director:	Carol S. Auletta, B.A., D.A.B.T.
Supervisor:	Donna L. Blaszcak, B.S.
Technician-In-Charge:	Nancy Minczeski, B.A.
Study Monitor: (Report Preparation)	Carol Loder, B.S.

IV. MATERIALS:

A. Test Animals: Albino Rats

Strain:	Sprague-Dawley CD^R
Reason for Selection:	Standard laboratory animal
Supplier:	Charles River Breeding Laboratories, Inc. Wilmington, Massachusetts
Number:	Range-finding: Twenty (one/sex/dose level) LD_{50} Determination: Forty (five/sex/dose level)
Age:	Young Adults
Weight: (pretest)	Males: 210 to 258 grams Females: 207 to 230 grams
Equilibration Period:	9 to 30 days
Observations:	All animals were checked for viability twice daily. Prior to assignment to study all animals received a physical examination to ascertain suitability for study.

Husbandry:

Housing:	Group-housed (six/cage) during equilibration. Individually housed during study.
Cages:	Suspended, stainless steel cages with wire mesh bottoms.

IV. MATERIALS:

Environmental Conditions:	Temperature: 68-76°F is considered an acceptable temperature range for rats; room temperature was monitored twice daily and maintained within this range to the maximum extent possible.
	Humidity: monitored daily
	Light Cycle: 12 hours light, 12 hours dark
Food:	Purina Laboratory Chow, ad libitum
Water:	Automatic watering system, ad libitum Municipal water supply (Elizabethtown Water Company)
Identification:	Each animal was identified with a monel ear tag bearing a unique number prior to testing.
Selection:	All animal numbers from each shipment of animals were placed in random order, using a random numbers table. A separate list was generated for males and females. Animals for study were selected by following these lists. Any animals considered unsuitable because of poor health or outlying body weight were excluded and the succeeding number was used.
B. Test Material:	C-253
Description:	Light amber crystalline slurry
Date of Receipt:	September 28, 1981
Received From:	Celanese Corporation
Storage:	Below 32.2°C in amber glass container

APPENDIX A

AN ACUTE INTRAPERITONAL TOXICITY STUDY IN RATS

GLOSSARY - NEUROLOGIC EVALUATIONS

The following is a description of selected terminology and procedures used to assess neurologic function in the rat.

1. Central Nervous System:

   a. Tremors - Involuntary, purposeless, oscillatory movements which result from alternate contraction of opposing muscle groups.

   b. Twitches - Brief, coarse, involuntary muscle contractions which cause the animal to abruptly jerk or twitch its limbs and/or body. They are frequently a precursor to convulsions.

   c. Convulsions - These are identified by type:

   1) Clonic-Type Convulsions - Convulsions with alternated contraction and relaxation of the voluntary muscles. Some examples:

      A coordinated, unsymmetrical convulsion with natural, purposeful-like movements, e.g., "running".

      Repetitive symmetrical jerks or twitches of the limbs, often accompanied by mild clonus or leading to a severe convulsion.

      Clonus of the jaws only.

      A seizure where the animal repeatedly "pops" into the air.

      A terminal clonic convulsion resulting from respiratory failure.

   2) Tonic-Type Convulsions

      Persistent contraction and spasm of a set of voluntary muscles. Typically a sustained extension of the hindlimbs, usually preceded by tonic flexion.

      A seizure in which the head, body and limbs are rigidly extended and arched backwards or forward.

3) Miscellaneous - Type Convulsions

a) Rock and Roll - A convulsion in which the animal is prostrate on its back and rocks from side to side in a seeming effort to right itself, occasionally rolling over (overshooting) and continuing to rock again.

b) Sitting-Up - A convulsion in which the animal sits upright on its hindlimbs during the seizure; a sitting-up seizure in which the forelimbs are held together or crossed in an attitude resembling prayer.

2. Behavior (Bizarre or sterotyped behaviors):

a. Head Flicking - head shaking or backward flip of head.

b. Head Searching - a stereotyped, repetitive turning of the head from side to side, as though searching the environment.

c. Hallucinatory-Like - behavior in which the animal appears to be responding to objects not present, e.g., visual tracking or fear-withdrawal.

d. Compulsive Biting - usually of the grid floor.

e. Compulsive Licking - usually of the cage walls.

f. Self-Destructive Biting - usually biting of toes with bleeding.

g. Prancing Forelimbs - Restless shifting from one forelimb to the other, with slight turning of the body from side to side.

3. Posture:

This reflects both the behavioral and neurologic state of the animal, since tail and pelvic elevation are usually increased by excitation or rigidity and decreased by stupor or flaccidity. It is evaluated, in the main, during forward movement of the animal.

a. Pelvic Elevation - The elevation of the abdomen from the surface during forward movement of the animal. It primarily reflects the limb position-its extension or flexion. A crouched posture or abnormal head position may also be present.

b. Tail Elevation - This is observed during the forward movement of the animal; the tail tends to be lower when the animal is at rest.

c. Limb Rotation - Any abnormal rotation of the hindlimbs from a vertical stance.

4. Gait:

a. Ataxia/Waddling - This results from an inability of the truncal, pelvic and limb muscles to move in unison, so that the animal tends to excessively sway, rock or lurch to the side as it proceeds forward and is variously unable to walk a straight line. Lateral wobbling movements of the pelvis are due to weakness of the gluteal muscles.

b. Circling - Tendency to move in circles around and along objects, or in an open environment.

c. Other:

1) Steppage - Due to paralysis of the muscles of dorsiflexion of the foot or toes, the animal drags its forelimbs in walking, walks on its knuckles, or lifts its forelimbs unusually high to avoid dragging its toes over the ground (spino-muscular involvement).

2) Spastic - Shuffling gait with legs rigidly extended and not lifted during movement. When severe, the animal may walk on tip-toe (cortico-spinal involvement).

3) Dysmetric - Incoordinate movement with a coarse tremor due to overshooting goal and oscillating back and forth trying to reach it (cerebellar or posterior column involvement).

4) Duck-Walk - An involvement of the hindlimbs in which the animal walks with adducted thighs, laterally extended legs and on tip-toe, causing it to assume a crouched posture (produced by narcotic analgesics).

5) Scissor - The forelimbs cross over in extension (in front of one another) due to marked spasticity and adductor hypertonicity, and the animal moves on the balls of its feet (cortico-spinal impairment).

5. Muscle Tone:

This reflects both the behavioral and neurologic state of the animal, increasing with apprehension or excitement and decreasing with relaxation. It is scored in terms of the relative presence of muscle resiliency (resistence to compression) or flaccidity (softness with continuing cavity deformation after compression).

a. Body Tone - This is determined by compressing the sides of the animal between the lower thorax and pelvis several times at approximately one second intervals, using the thumb and index finger.

b. Limb Tone - The animal is restrained in supine position and the tip of the index finger gently pushed against the plantar surface of each hindpaw several times to determine its resistance to passive flexion.

6. Reflexes:

a. Toe Pinch - A leg withdrawal response (ipsilateral flexor reflex) after light compression of the lateral surface of the mid-digit of each foot with a forceps.

b. Pupil - Normally the pupil will constrict on sudden exposure to intense light. Persistent constriction or no response to light are considered abnormal.

c. Righting - The animal is placed on its back, and allowed to right itself. Sluggish or incomplete righting is considered abnormal.

d. Visual Placing - The animal is lifted vertically, by mid-tail, approximately 15 cm. above an inverted cage, and then lowered to elicit the visual placing response, usually characterized by an extension of both fore-and-hindlimbs before contact.

e. Corneal - The blink or eye-closure response of each eye to light tactile stimulation of the cornea.

f. Startle - A sudden body jerking movement of the animal in response to a finger snap.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
Rhône-Poulenc Inc.
CN 7500
Cranberry, New Jersey 08512-7500

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 0 8 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and **refer to the reverse side of this page for "EPA Information Requests"** .

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12099A

Triage of 8(e) Submissions

Date sent to triage: MAY 0 9 1995

NON-CAP CAP

Submission number: 120994

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1,2 **pages** 1,2

Notes:

Contractor reviewer : PJR **Date:** 4/25/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 - 12099 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/04/92 OTS DATE: 09/21/92 CSRAD DATE: 03/10/95

CHEMICAL NAME:

CAS#
3524-68-3

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
(0209)	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

ATOX

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
(N TRANSMIT)

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT

TOXICOLOGICAL CONCERN:
LOW
MED
(HIGH)

USE:

PRODUCTION:

COMMENTS:

-CPSS- 0928951301

0 0 0 0 0 0 0 0 0 0 0
> <ID NUMBER>
8(E)-12099A

> <TOX CONCERN>
H

> <COMMENT>
ACUTE INTRAPERITONEAL TOXICITY IN RATS IS HIGH CONCERN BASED ON AN LD50 OF 25 MG/KG. DOSE (MG/KG) AND MORTALITY: 3 (0/5 M, 0/5 F), 10 (0/5 M, 0/5 F), 30 (5/5 M, 3/5 F), AND 100 (5/5 M, 5/5 F). A RANGE-FINDING STUDY WAS ALSO CONDUCTED USING 4 ANIMALS (2/SEX) AT EACH DOSE LEVEL. DOSE (MG/KG) AND MORTALITY: 3 (0/4), 10 (1/4), 30 (3/4), 100 (4/4), AND 300 (4/4). NEUROLOGICAL SIGNS INCLUDED ATAXIA, BODY AND LIMB FLACCIDITY, ABNORMAL STARTLE, RIGHTING AND VISUAL PLACING REFLEXES, CONVULSIONS, COMPULSIVE BITING, PUPILS NOT RESPONDING TO LIGHT, AND UNCOORDINATED EYE MOVEMENT. CLINICAL SIGNS INCLUDED OCULAR AND NASAL DISCHARGE, PROSTRATION, DYSPNEA, SOFT STOOL, PILOERECTION, SWOLLEN EYELIDS, HYPOPNEA, URINARY AND FECAL STAINING, UNTHRIFTY COAT, HYPOACTIVITY, DECREASED FOOD INTAKE, BLANCHING, EMACIATION, AND DISTENDED ABDOMEN. NECROPSY REVEALED CHANGES IN THE LUNGS, LIVER, STOMACH, SPLEEN, INTESTINES, ADRENALS, AND BODY CAVITY.

$$$$